7.4.2 Body Weights:

At the end of the observation period, the animals were weighed.

7.4.3 Euthanasia:

At the end of the study, the animals were returned to the general colony.

8.0 EVALUATION CRITERIA

8.1 Evaluation of Data:

After the 72 ± 2 hours grading, all erythema grades plus edema grades from 24 ± 2 hours, 48 ± 2 hours, and 72 ± 2 hours were totaled separately for each test article or vehicle control for each individual animal. To calculate the score of a test article or vehicle control on each individual animal, divide each of the totals by 15 (3 scoring time points × 5 test or vehicle control injection sites). To determine the overall mean score for each test article and each corresponding vehicle control, add the scores for the three animals and divide by three. The final test article score was obtained by subtracting the score of the vehicle control from the test article score. The requirements of the test will be met if the difference between the test article mean score and the vehicle control mean score is 1.0 or less. If at any observation period the average reaction to the test article is questionably greater than the average reaction to the vehicle control, the test will be repeated using three additional rabbits.

8.2 Control of Bias Statement:

The study as designed employed methodology to minimize uncertainty of measurement and to control bias for data collection and analysis, which included but was not limited to: concurrent control data, system suitability assessment, randomization, and method controls such as blanks and replicates.

9.0 RESULTS

9.1 Animal Weights:

All of the animals increased in weight (Table 1).

9.2 Clinical Observations:

None of the animals exhibited overt signs of toxicity at any of the observation points (Table 1).

The sites injected with the test article did not show a significantly greater biological reaction than the sites treated with the control article (Table 2). The difference of the overall mean score between the test article and the control article was 0.0.

10.0 CONCLUSION

The USP 0.9% Sodium Chloride for Injection (NaCl) and Cottonseed Oil (CSO) extracts of the test article, 19 Samples numbered consecutively from 1 - 19/ lot # 1-1121BF, were evaluated for their potential to produce irritation after intracutaneous injection in New Zealand White rabbits. The test article sites did not show a significantly greater biological reaction than the sites injected with the control article.

Based on the criteria of the protocol, the test article meets the requirements of the ISO 10993-10 and ISO 10993-23 guidelines.

8.2 Control of Bias Statement:

The study as designed employed methodology to minimize uncertainty of measurement and to control bias for data collection and analysis, which included but was not limited to: concurrent control data, system suitability assessment, randomization, and method controls such as blanks and replicates.

9.0 RESULTS

9.1 Animal Weights (Table 3):

All animals were within the specified range of body weights (300–500 g) at the initiation of the study (Day 0).

9.2 Clinical Observations (Table 3):

No systemic signs of toxicity were observed in treated or control animals.

9.3 Sensitization (Table 4):

None of the treated (NaCl or CSO extracts) or negative control animals exhibited any reaction at the challenge (0% sensitized). The positive control article elicited discrete (Grade 1) reactions in four animals and a moderate (Grade 2) reaction in one animal (100% sensitized).

10.0 CONCLUSION

The USP 0.9% Sodium Chloride for Injection (NaCl) and Cottonseed Oil (CSO) extracts of the test article, 19 Samples numbered consecutively from 1 – 19/ lot # 1-1121BF, elicited no reaction at the challenge (0% sensitization), following an induction phase. Therefore, as defined by the grading scale of the USP, the test article is classified as a non-sensitizer.

Based on the criteria of the protocol and these results, the test article meets the requirements of the ISO 10993–10 guidelines.

11.0 RECORDS

- Original raw data will be archived by Toxikon Corporation.
- The original final report and any report amendments will be archived by Toxikon Corporation.
- A copy of the final report and a copy of the protocol and any protocol amendments or deviations will be forwarded to the Sponsor.
- The test article will be returned by Toxikon.
- Test article retention upon study completion is the responsibility of the Sponsor.

12.0 CONFIDENTIALITY AGREEMENT

Per corporate policy, confidentiality shall be maintained in general, and in specific accordance with any relevant agreement specifically executed between Toxikon and the Sponsor.

Nelson Labs.
A Sotera Health company

Sponsor:
Ion Clairety, LLC

MEM Elution GLP Report

Test Article:	lot # 1-1121BF #11
Purchase Order:	2-1121
Study Number:	1478172-S01
Study Received Date:	22 Dec 2021
Test Started Date:	13 Jan 2022
Test Finished Date:	17 Jan 2022
Testing Facility:	Nelson Laboratories, LLC 6280 S. Redwood Rd. Salt Lake City, UT 84123 U.S.A.
Test Procedure(s):	Standard Test Protocol (STP) Number: STP0032 Rev 11
Deviation(s):	None

Summary: The Minimal Essential Media (MEM) Elution test was designed to determine the cytotoxicity of extractable substances. An extract of the test article was added to cell monolayers and incubated. The cell monolayers were examined and scored based on the degree of cellular destruction. All test method acceptance criteria were met.

Results:
Test Article:

Dilution	Results Pass/Fail	Scores				Extraction Ratio	Amount Tested / Extraction Solvent Amount
		#1	#2	#3	Average		
Neat	**Fail**	3	3	3	3		
1:2	**Pass**	2	2	2	2		
1:4	**Pass**	0	0	0	0	3 cm^2/mL	60 cm^2 / 20 mL
1:8	**Pass**	0	0	0	0		
1:16	**Pass**	0	0	0	0		

Note: An additional 4 mL of media was added to account for absorbency.

Study Director Brittany Love

Study Completion Date

1478172-S01